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09/654,948	09/01/2000	J. Leighton Read	2719.2003-000	7877

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EXAMINER

PONNALURI, PADMASHRI

ART UNIT	PAPER NUMBER
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1639

DATE MAILED: 10/29/2003

26

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary

Application No.

09/654,948

Applicant(s)

Pirrung et al

Examiner

Padmashri Ponnaluri

Art Unit

1639



-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136 (a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

- 1) ☒ Responsive to communication(s) filed on Apr 28, 2003
- 2a) ☒ This action is **FINAL**. 2b) ☐ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11; 453 O.G. 213.

Disposition of Claims

- 4) ☒ Claim(s) 172-184, 186, and 188-192 is/are pending in the application.
- 4a) Of the above, claim(s) _____ is/are withdrawn from consideration.
- 5) ☐ Claim(s) _____ is/are allowed.
- 6) ☒ Claim(s) 172-184, 186, and 188-192 is/are rejected.
- 7) ☐ Claim(s) _____ is/are objected to.
- 8) ☐ Claims _____ are subject to restriction and/or election requirement.

Application Papers

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on _____ is/are a) ☐ accepted or b) ☐ objected to by the Examiner.
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
- 11) ☐ The proposed drawing correction filed on _____ is: a) ☐ approved b) ☐ disapproved by the Examiner.
If approved, corrected drawings are required in reply to this Office action.
- 12) ☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

- 13) ☐ Acknowledgement is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
a) ☐ All b) ☐ Some* c) ☐ None of:
1. ☐ Certified copies of the priority documents have been received.
2. ☐ Certified copies of the priority documents have been received in Application No. _____.
3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).
*See the attached detailed Office action for a list of the certified copies not received.
- 14) ☐ Acknowledgement is made of a claim for domestic priority under 35 U.S.C. § 119(e).
a) ☐ The translation of the foreign language provisional application has been received.
- 15) ☒ Acknowledgement is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

- 1) ☐ Notice of References Cited (PTO-892) 4) ☐ Interview Summary (PTO-413) Paper No(s). _____
- 2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948) 5) ☐ Notice of Informal Patent Application (PTO-152)
- 3) ☐ Information Disclosure Statement(s) (PTO-1449) Paper No(s). _____ 6) ☐ Other: _____

Art Unit: 1639

DETAILED ACTION

1. The response filed on 4/23/03 and the supplemental response filed on 4/28/03 have been fully considered and entered into the application.
2. The 'incorporation by subject matter of related applications' in the specification filed on 7/9/01, as new matter made in the previous office action mailed on 10/18/02 has been withdrawn.
3. Applicants arguments regarding the obviousness type double patenting of claims over US Patent 5,143,854 have been considered. In view of restriction of the method of preparing sequences on solid support, made in the 854 patent the rejections of record have been withdrawn. In the previous office action mailed on 10/18/02 has inadvertently included that the rejection has been ~~mentioned~~^{maintained} in item 11. Examiner apologizes for the confusion caused by the error.
4. Claims 172-184, 186, 188-192 are rejected under 112, first paragraph (written description) for the reasons set forth in the previous office action mailed on 12/18/01.
5. Claims 172-184, 186, 188-192 are rejected under 112, first paragraph (scope enablement) for the reasons set forth in the previous office action mailed on 12/18/01.
6. The provisional obviousness-type double patenting rejection of claims 172-209 over US Patent application 08/563,759 has been maintained for the reasons of record set forth in the previous office action mailed on 12/18/01.

Art Unit: 1639

7. The obviousness-type double patenting rejection of claims 172-209 over US Patent 6,379,895 B1 has been maintained for the reasons of record set forth in the previous office action mailed on 10/18/02.

Response to Arguments

8. The text of those sections of Title 35, U.S. Code not included in this action can be found in a prior Office action.

9. Claims 172-184, 186, 188-192 are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

The instant claims briefly recite a method of synthesizing a polypeptide array, wherein said array comprises at least two different polypeptides immobilized on a substrate, comprising: a) contacting said surface with a first protected group; b) contacting the said surface with a second protected amino acid; and c) repeating the above steps until at least two different polypeptides are formed at known location on said substrate surface.

The specification description is directed to the use of photo lithographic techniques in the methods of making arrays of chemical compounds such as peptides or oligonucleotides, which clearly do not provide an adequate representation regarding the open ended method of synthesizing a polypeptide array of the instant claims. And the use of photo lithographic technique is critical or essential to practice the instant invention.

With regard to the description requirement, Applicants' attention is directed to The Court of Appeals for the Federal Circuit which held that a "written description of an invention involving a chemical genus, like a description of a chemical species, 'requires a precise definition, such as by structure, formula [or] chemical name,' of the claimed subject matter sufficient to distinguish it from other materials." *University of California v. Eli Lilly and Co.*, 43

Art Unit: 1639

USPQ2d 1398, 1405 (1997), quoting *Fiers v. Revel*, 25 USPQ2d 1601, 1606 (Fed. Cir. 1993) (bracketed material in original)[The claims at issue in *University of California v. Eli Lilly* defined the invention by function of the claimed DNA (encoding insulin)].

Although directed to DNA compounds, this holding would be deemed to be applicable to any compound or methods of making the compounds or arrays; which requires a representative sample of methods of making the compounds and/or a showing of sufficient identifying characteristics; to demonstrate possession of the claimed generic(s).

Additionally, the narrow scope of examples directed to photolithography technique in making arrays are clearly not representative of the scope of the claimed method of synthesizing array of polypeptides.

10. *Applicant's arguments regarding the written description rejection of record filed on 4/23/03 and 4/28/03 have been fully considered but they are not persuasive.*

Applicants argue that the instant claims are based in part on the inventive concept that polymers can be synthesized by combinatorial methods by the selective application of an activating agent, which will remove protecting groups and subsequently allow growth of a polymer on specific regions of a substrate. Although the methods are largely exemplified by the use of a mask to direct light to specific regions of substrate, where it removes photosensitive protecting groups, the specification clearly teaches that other activating agents and protecting groups can be employed in a similar manner.

Applicants arguments have been considered and are not persuasive, since the instant specification sufficiently disclose the use of other activating agents other than light in the

Art Unit: 1639

claimed method of synthesizing a polypeptide array. Even though the specification discloses other means of protecting and deprotecting reagents, the specification nowhere teaches "selective protection or deprotection of reagents on defined locations of the substrate" using any other means of agents useful in the method of synthesizing array of polypeptides.

Applicants further argue that specification in page 19, 21 and 133 disclose the various other activating agents could be used in the claimed method. However, nowhere in the specification it has been disclosed that the polymer (peptide) arrays have been prepared using activating agents other than light.

Applicants further argue that activating agents other than the light, along with appropriate protecting groups, for synthesis of a single peptide species on a solid support were well known in the art at the time of the invention. Applicants arguments have been considered and are not persuasive, since the instant specification specifically teaches the use of photolithographic techniques in the synthesis of polypeptide arrays. In addition the specification in page 10 teaches that 'by using lithographic techniques disclosed herein, it is possible to direct light to relatively small and precisely known locations on the substrate. It is, therefore, possible to synthesize polymers of a known chemical sequence at known locations on the substrate.' The specification does not specifically teach the use of activating agents other than light in the instant claimed method steps of synthesizing a polypeptide array.

Applicants in the arguments further refer to several sections of the specification which are specific to array synthesis. And rely on the disclosure that 'other activating agents are well

Art Unit: 1639

known in the art at the time the instant application's effective filing date.' applicants arguments have been considered and as in the supra response, there are so many other well activating agents are known in the art at the time th invention was made however, it is not known that these activating agents are used in array synthesis as claimed. Thus, the instant specification lacks written description for the claimed method. The rejections of record have been maintained.

11. Claims 172-184, 186, 188-192 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for photo lithographic method in protection and deprotection steps of the instant method, does not reasonably provide enablement for the use of other techniques such chemical or magnetic methods. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the invention commensurate in scope with these claims.

The instant claims briefly recite a method of synthesizing a polypeptide array, wherein said array comprises at least two different polypeptides immobilized on a substrate, comprising: a) contacting said surface with a first protected group; b) contacting the said surface with a second protected amino acid; and c) repeating the above steps until at least two different polypeptides are formed at known location on said substrate surface.

The specification disclosure does not have a sufficient enabling disclosure for the use of chemical or thermal or magnetic techniques to remove the protecting groups from the compounds so that activated region on the surface is formed.

The factors to be considered in a determination of undue experimentation are disclosed in *In re Wands* (U. S. P. Q. 2d 1400: CAFC 1988) which include: the quantity of experimentation necessary; . the amount of direction or guidance presented; the presence or absence of working examples; . the nature of the invention; the state of the prior art; the predictability of the art; and the breadth of the claims.

Art Unit: 1639

A number of factors would prevent one of ordinary skill in the art from practicing (making and using) the invention without undue experimentation, which are summarized as follows:

- a. The specification fails to give adequate direction and guidance as to the means of synthesizing arrays of polypeptides using techniques other than photolithographic technique. The specification discloses selective deprotection and/or activation with photolithography. The specification discloses that the photolithographic technique makes it possible to direct light to relatively small and precisely known location on the substrate.
- b. The working examples directed to the use of photolithographic technique in making arrays of polypeptides or nucleotides.
- c. The breadth of the claims are open-ended regarding method of making the arrays.
- d. The state of the prior art at the time the invention was made is such that synthesis of array of compounds on a substrate, by selective protecting and deprotecting (using chemical or magnetic methods) in general are known to be difficult or unknown.
- e. The art is inherently unpredictable because organic synthesis of peptide array on a substrate and selective protecting and or deprotecting of compounds using chemical or the thermal methods is not possible without using other methods (such as masking using barriers).

In view of the quantity of experimentation necessary, the limited working examples, the unpredictability of the art, the lack of sufficient guidance in the specification, it would take undue trials and errors to practice the claimed invention.

12. Applicant's arguments filed on 4/24/03 and 4/28/03 have been fully considered but they are not persuasive.

Applicants argue that the use of chemical, thermal and magnetic methods in protecting and deprotecting compounds as part of synthesizing a single polypeptide species on a solid support were known in the art at the time the invention was made. Applicants arguments have

Art Unit: 1639

been fully considered and are not persuasive, since the use of thermal and magnetic energy in synthesis of individual compounds on a solid support are known, however it is known at the time the invention was made to make polypeptide arrays as in the instant claims.

*Applicants argue that exhibit B, US Patent 5,547,839 which is incorporated by reference, discloses a solvent tight barrier, and Figure 11 of Exhibit b shows a schematic diagram of a reactor chamber formed by a substrate sealed to a an apparatus comprising entry and exit points for reagents. Applicants arguments along with the exhibit B have been considered and are not persuasive. Applicants arguments using Exhibit are irrelevant to the instant claimed method rejections of record (whether activating agents other than light are used in the claimed method), however the arguments are answered briefly. The brief description of figure 11 of the exhibit B discloses that **"Fig 11 illustrates a functionalized apparatus for performing the scanning steps and sequencing reaction steps."** Thus, the apparatus in figure 11 of Exhibit is not relevant to the claimed method of synthesis of array of polypeptides on a sold substrate. Applicants further arguments that "one skilled in the art would recognize the use of a reaction chamber having a smaller surface area than the substrate, such that one could position the chamber selectively activate regions of the substrate" does not overcome the rejections of record.*

Applicants in the response filed on 4/28/03 argue that the figure 11 of exhibit B discloses a reaction chamber with necessary tubing and valves to control the entry and exit of the reagents. Applicants refer to column 28, lines 27-38. Applicants further argue that "one skilled in the art would recognize that the size of the reaction chamber can be varied to control

Art Unit: 1639

how large an area on the substrate is exposed to reagents at a particular time. Also one skilled in the art would recognize that reaction chamber of varying sizes could be utilized at different stages of polypeptide array synthesis.” Applicants arguments have been considered and are not persuasive, since the instant claims are not drawn to size of synthesis surface or the amount of reagents used in the claimed method. The instant claimed method does not use different solid substrates in the synthesis of polypeptide array as in applicants response. The instant claim recites the use of ‘first selectively activated region’ and ‘second selectively activated regions of the substrate’ ‘known locations of the substrate’ which are considered are present on one single solid support. In the instant claimed it is interpreted that the solid substrate has been divided into multiple regions, and the reactions are conducted in specific regions of a single solid support which is different from applicants arguments and referral to figure 11 of Exhibit B.

Applicants arguments regarding the use of a beam in deprotecting and deprotecting have been considered and are not persuasive, since the arguments not based on the instant claim limitations. Applicants in the supplemental response filed on 4/28/03 argue that use of numerous lithographic methods are enabled. In support the assertion, applicants refer to Chapter 4 of VLSI technology, second edition by S. M. Sze. And further argue that VLSI technology contains a discussion of various other lithographic techniques.

Applicants arguments regarding chapter 4, VLSI technology reference has been considered. However, applicants discussion of several different lithographic methods have been considered and are not persuasive because the instant claimed methods are not drawn to the use

Art Unit: 1639

of specific lithographic techniques, and further even if the techniques are known in the art it was not known at the time the invention was made to use lithographic techniques in the instant method of making polypeptide arrays. And as in applicants arguments if the activating agents are known in the art and one skilled in the art at the time the invention was made knows how to use the agents in polypeptide array synthesis, does applicants mean that it is obvious to one skilled in the art to make polypeptide array of the claimed method. Applicants arguments have been considered and are not persuasive.

13. Applicant's arguments filed on 4/24/03 regarding the obviousness type double patenting rejection over US Patent 6,379,895 have been fully considered but they are not persuasive. Applicants respond that 'applicants will consider the filing of terminal disclaimer to overcome the rejections as appropriate upon notice of allowable subject matter... This will permit, applicants to assess the rejections in the view of claims as ultimately indicated allowable, since it is possible that the claims may change during the course of prosecution.' Applicants response has been considered and the rejections of record have been maintained for the reasons of record. The rejections would be withdrawn upon filing of terminal disclaimer and entered into the application.

14. The obviousness-type double patenting rejection of claims over U S Patent application 08/563,759 (now US Patent 6506558) has been maintained for the reasons of record in view of absence of response filed by applicants.

Art Unit: 1639

15. No claims are allowed.

16. **THIS ACTION IS MADE FINAL.** Applicant is reminded of the extension of time policy as set forth in 37 CAR 1.136(a).

A shortened statutory period for reply to this final action is set to expire **THREE MONTHS** from the mailing date of this action. In the event a first reply is filed within **TWO MONTHS** of the mailing date of this final action and the advisory action is not mailed until after the end of the **THREE-MONTH** shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CAR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than **SIX MONTHS** from the mailing date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to P. Ponnaluri whose telephone number is (703) 305-3884. The examiner is on **Increased Flex Schedule** and can normally be reached on Monday to Friday from 7.00 AM to 3.30 PM.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Andrew Wang, can be reached on (703) 306-3217. The fax phone number for the organization where this application or proceeding is assigned is (703) 872-9306.

Art Unit: 1639

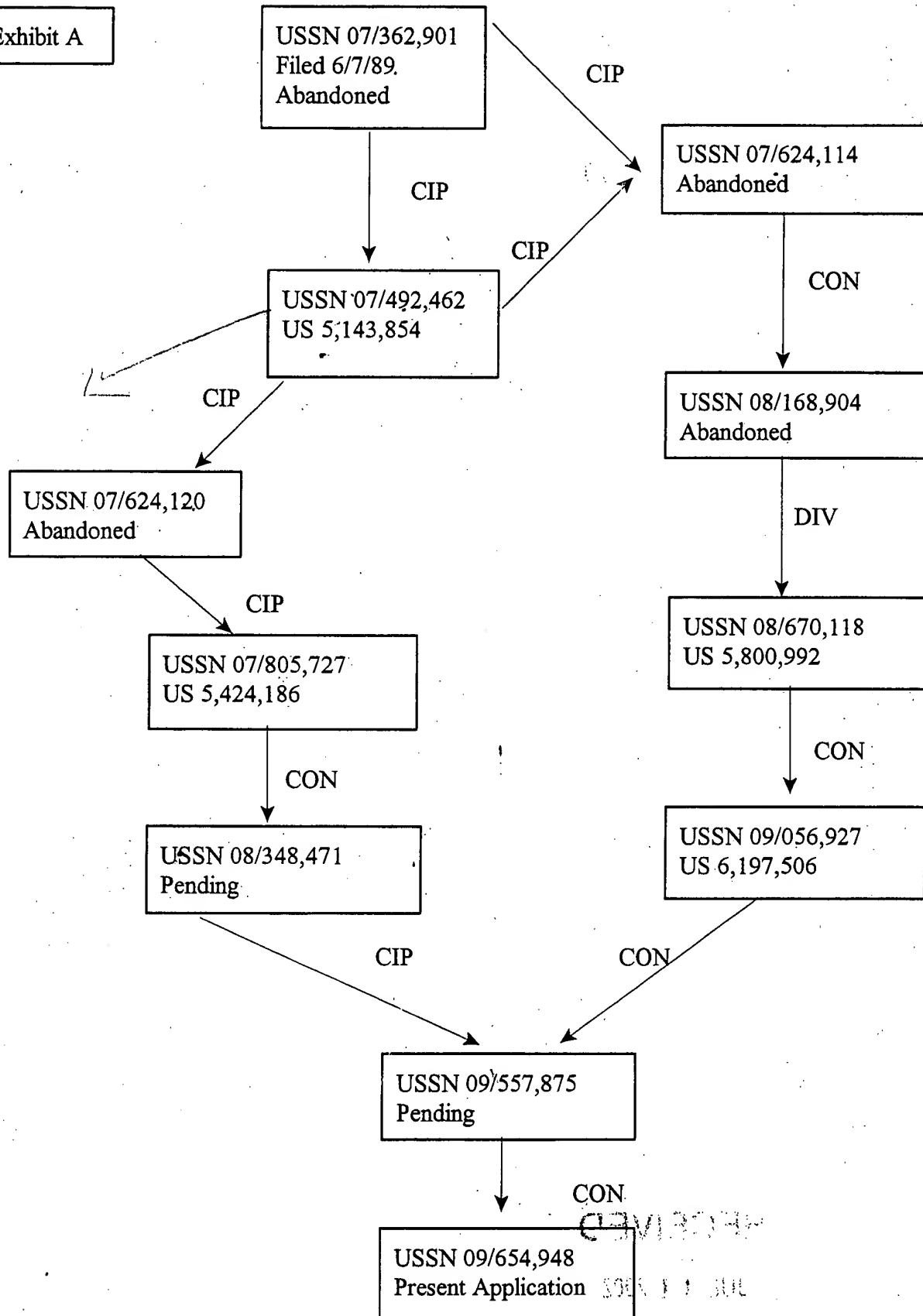
Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is (703) 308-0196.

P. Ponnaluri
Primary Examiner
Technology Center 1600
Art Unit 1639
24 October 2003



PADMASHRI PONNALURI
PRIMARY EXAMINER

Exhibit A



DOES NOT REFLECT 405

EXHIBIT

A